REMARKS

Reconsideration is requested.

Claims 35, 37-38, 41-44 and 46-64 are pending. Claims 38, 48-56 and 62-64 have been withdrawn from consideration. Claims 1-34, 36, 39-40 and 45 have been canceled, without prejudice.

The Examiner's comments regarding the PTO 1449 Form filed July 23, 2004, are noted. A Request for return of an initialed copy of the previously-filed PTO 1449 Form was filed September 11, 2006. A copy of the previously-cited documents, and a listing of the same with the further document described below, is attached in the event the same is what is further required by the Examiner. The Office Action dated August 15, 2006 does not indicate that a further copy of the documents is required however the same are submitted herewith to expedite acknowledgement of the consideration of the documents. Return of an initialed copy of the attached PTO 1449 Form listing the documents, pursuant to MPEP § 609, is requested.

The claimed invention define a rodent having a mutated LAT gene coding for a mutant LAT protein, wherein the sequence of said mutant LAT protein differs from a wild type sequence by a single mutation of a tyrosine located at position 136 of the mouse LAT protein sequence, said rodent being homozygous for the mutated LAT gene or a carrier of a null allele of the LAT gene, and said mutant LAT protein leading to an exaggerated TH2 cell differentiation.

The claims find support, for example, in now-canceled claims 36, 40 and 45, and in page 5 (lines 23-35), page 6 (lines 1-23) and page 7 (lines 8-15) of the specification. No new matter has been added.

Claims 63 and 64 specify that the mutant LAT protein contains a single mutation of the tyrosine Y136. Support for the recitation is found, for example, at page 7, line 11 of the specification.

Rejoinder and allowance of any claim defining a method of making and/or using a product defined by an allowable claim, at an appropriate time, are requested.

The claims have been amended without prejudice or disclaimer and solely in order to facilitate reconsideration of this application. In particular, applicant reserves his right to file a continuation and/or divisional application(s), and the present amendment shall not be considered as an admission of the objection or as a waiver of any subject matter.

To the extent not obviated by the above amendments, the Section 112, first paragraph, rejections of claims 35-37, 39-47 and 57-61 is traversed. Reconsideration and withdrawal of the rejection are requested in view of the above and the following further comments.

As noted above, the claims describe a rodent. The specification is believed to adequately describe and teach one of ordinary skill how to make and use the claimed invention. Specifically, for example, the specification teaches that the claimed invention may be carried out using mammals, in particular rodents:

> "Preferably, said non-human animals according to the invention are mammals, and in particular, they are rodents." (see page 6, lines 19-20).

One of ordinary skill in the art will appreciate that the results provided in the specification with mice demonstrate possession of the claimed invention and that the

manner of making and using the exemplifications of the disclosure may be extrapolated to different rodents without undue experimentation.

The claims specify, as suggested by the Examiner, that the rodents of the claims are homozygous for the mutated LAT gene or carry a null allele of the LAT gene. Support for the recitation, as acknowledged by the Examiner, can be found, for example by page 6, lines 21-23 of the specification.

The applicants further believe that the specification describes exaggerated TH2 cell differentiation. One of ordinary skill in the art will appreciate a correlation between i) an increase of the IgE and IgG1 secretions and of eosinophilia, and ii) an increase in TH2 cell differentiation.

Attached for the Examiner's consideration in this regard are the following scientific articles:

"Induction of T helper type 2 immunity by a point mutation in the LAT adaptor" – Science – Aguado et al., 14 June 2002, Vol. 296; and

"The Th2 lymphoproliferation developing in Lat^{Y136F} mutant mice triggers polyclonal B cell activation and systemic autoimmunity" – The Journal of Immunology – Genton et al., 2006, 177:2285-2293.

Aguado et al. describes, in Figure 4 C, a 10 000 fold increase of the IgE secretion and a 200 fold increase of the IgG1 secretion in mutant mice compared to the secretion observed in wild-type mice. This reflects a massive maturation of plasma cells which in turn reflects an exaggerated TH2 differentiation. This differentiation is also apparent through tissue eosinophilia (see abstract) and the enlargement of spleen and large nodes of mutant mice (see, page 2037, second paragraph and Figure 1). Figures

3 A and B further show the exceptional Th2 cell differentiation of CD4 cells which proliferate in the LATY136F mice.

Genton et al., confirms the results described in the present specification, i.e., the exaggerated TH2 cell differentiation observed in LATY136F mice:

> "Lat^{Y136F} knock-in mice harbor a point mutation in Tyr^{136} of the linker for activation of T cells and show accumulation of Th2 effector cells and IgG1 and IgE hypergammaglobulinemia." (see abstract).
>
> "Taken together, our results show that Lat^{Y136F} T cells induce an MHC class II-independent polyclonal B cell response with all the B cell populations found in a physiological immune response. This Th2-mediated disease leads to increases in polyclonal IgG1 and IgE, a proportional increase in autoantibodies and severe systemic disease, including nephritis." (see page 2292, last paragraph before the acknowledgments).

The above and attached are submitted to demonstrate that the claims are supported by an adequate written description which teaches one of ordinary skill in the art how to make and use the claimed invention.

Withdrawal of the Section 112, first paragraph, rejections are is requested.

The Section 112, second paragraph, rejection of claims 36, 37, 42-44, 47 and 58-61 is obviated by the above amendments. Withdrawal of the rejection is requested.

The Section 102 rejection of claims 47 and 57-61 over Sommers (Journal of Experimental Medicine, 194(2), 135-142), is traversed. Reconsideration and withdrawal of the rejection are requested in view of the following distinguishing comments.

As noted previously in the applicants Response of May 22, 2006, Sommers et al. states that "no mature T cells were present" in the studied LAT "knock-in" mutant mice having a mutation of the four distal tyrosines.

This document does not describe a Lat^{Y136F} rodent according to the invention, having a single mutation, and does not describe nor suggest the phenotype that should be observed in such a rodent, wherein the mutant LAT protein leads, on the contrary, to an exaggerated TH2 cell differentiation.

The Examiner is further requested to review the attached Aguado et al. which describes the generation of the knock-in mice according to the invention, having a mutation that replaced tyrosine 136 with phenylalanine (Y136F). This paper further refers, on page 2036, right column, to the Sommers et al. paper of 2001.

The attached Aguado et al. is submitted as evidence that mutant rodents according to the invention and mutant mice according to Sommers et al. have been obtained using different protocols and lead to different observations. Specifically, the presently claimed invention is directed to a single particular mutation, whereas Sommers et al. generate

> "Mice deficient in LAT (LAT-/-) or having a mutation of the four COOH-terminal tyrosine residues" (see page 2036, right column of Avoguado et al.).

In Sommers et al., the mutation of the four distal tyrosines leads to the arrest of thymocyte development while the presently claimed invention which involves the single Y136F mutation leads to an exaggerated TH2 cell differentiation. This result is not described or suggested by Sommers et al.

Withdrawal of the Section 102 rejection is requested.

The claims are submitted to be in condition for allowance and a Notice to that effect is requested. The Examiner is requested to contact the undersigned in the event anything further is required in this regard.

Respectfully submitted,

NIXON & VANDERHYE P.C.

By: /B. J. Sadoff/
B. J. Sadoff
Reg. No. 36,663

BJS:
901 North Glebe Road, 11th Floor
Arlington, VA 22203-1808
Telephone: (703) 816-4000
Facsimile: (703) 816-4100